

THE STUDY OF TETANUS INTOXICATION
AND ITS TREATMENT.

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PART I.

The Central Mechanism of Tetanus Rigidity.

Clinical experience in cases of tetanus intoxication with the universally bad results in its treatment, led me to undertake the study of the mechanism of tetanus intoxication.

One of the most striking features of tetanus intoxication is rigidity of the striated muscles. Here one finds an increase of muscle tonus without an increase in metabolic activity, as has been shown by FRÖHLICH & MEYER (7) who took electro-myographic currents as the standard of metabolic activity. These currents in the rigid muscles in tetanus intoxication were in no way different from those of resting muscles. This was confirmed by SEMERAU & WEILER (21) and also by LILJESTRAND & MAGNUS (15). Although HANSEN, HOFFMANN & WEISSACKER (9) demonstrated the presence of action currents in the rigid muscles, such currents were small compared with the action currents of muscles undergoing normal contraction. The glycogen content of rigid muscle in tetanus intoxication /

intoxication is not less than that in resting muscle -
ISHIZAKA (10).

These are indications that the mechanism of increased tonus in tetanus intoxication differs from the mechanism of ordinary muscle contraction.

The question now arises:- What is the mechanism of this rigidity in tetanus intoxication? It has been suggested that it is due to an alteration in the muscle itself - ZUPNIK (26).

GUMPRECHT (8) and MEYER & RANSOM (16) have maintained that the rigidity in tetanus is due to a toxic involvement of that segment of the spinal cord which supplies the muscles in question and FRÖHLICH & MEYER (7) have confirmed this statement against the objections of ZUPNIK (26) and of POCHHAMMER (17). The latter states that there is an alteration in the myelin sheath of the peripheral nerves. That the rigidity is due to an intoxication of the spinal cord has been proved by the fact that the rigidity cannot develop in a muscle which is not connected with the central nervous system.

The influence which the central nervous system exercises on the tonus in the development of tetanus rigidity was analysed in great detail by SPIEGEL (23). Attempting to show that the change cannot lie in the muscle /

muscle itself, he demonstrated that the reaction of the normal muscle and that of rigid muscle to immersion in dilute acids and then in salt solutions is similar, the changes in volume and weight in both cases being the same. Furthermore he found that there is not a lower tonus in the antagonists of the extensors, e.g., the antagonists of the gastrocnemius, which may explain the development of the extended position, and from this he was led to infer that the central nervous system acts directly on the rigid muscles.

There is no mechanism in tetanus intoxication which inhibits relaxation of muscles when stimulated; the stiff muscles when stimulated show the normal tracing of contraction and relaxation.

SHERRINGTON (22) demonstrated that tetanus toxin, when injected into an animal, changes the normal reciprocal inhibition of a muscle into excitation. From this one might infer that the action of tetanus toxin is in relation to the genesis of muscular rigidity.

It must be remembered, however, that the same transformation of reciprocal inhibition into excitation is also produced by strychnine, but strychnine does not cause the same type of rigidity as tetanus.

Rigid /

Rigid muscles in strychnine intoxication show the presence of action currents; on the other hand, rigid muscles in tetanus intoxication show very small action currents.

LILJESTRAND & MAGNUS (15) demonstrated that in the beginning of tetanus rigidity, as instanced in the triceps of a cat, flexor movements at the elbow are accompanied by relaxation of the extensors and that the change of reciprocal inhibition into excitation is only seen at a later stage in the development of the rigidity. From the above SPIEGEL (23) concluded that muscular rigidity in tetanus intoxication is due to a continuous irritation of the motor cells of the cord. This was in agreement with the experience of LILJESTRAND & MAGNUS (15) who pointed out that the destruction of the posterior nerve roots abolishes the rigidity.

There must therefore necessarily be present a continuous flow of proprioceptive impulses towards the motor cells of the cord to cause the rigidity in tetanus intoxication. The development of the muscular rigidity in tetanus intoxication is thus dependent on the central nervous system, the segmental motor centres being in a state of continuous irritation, in this way maintaining an increased muscular tonus. /

tonus.

It must now be considered whether the central mechanism of tetanus rigidity is only in the spinal cord or whether the supraspinal centres have an influence on the development of rigidity. In tetanus intoxication we find that there is a predilection for certain groups of muscles which show this increased tonus, such as the extensors of the limbs, (Fig. 1) of



Fig. 1.

the trunk, of the neck and of the masseter muscles. The selection of definite groups of muscles does not bring about any change in the muscles themselves. We have seen that no structural or chemical differences have ever been demonstrated in such muscles as compared /

compared with that of other striated muscles which could explain such a preference in the genesis of the rigidity. The study of general tetanus intoxication may lead one to suspect that the length of axones innervating different groups of muscles has some influence in determining the selection of muscles affected. The toxin, as we know from the work of MEYER & RANSOM (16), is absorbed by the ends of the axones and is conveyed to the central nervous system along the peripheral nerve parts, and in this way the centres with the shorter axones are those first to be affected. Such an explanation shows why the masseter muscle in man is always the first muscle in tetanus to be affected, but it does not explain why the extensors of the limbs, trunk and neck are affected in preference to the flexors, as both groups are innervated by axones practically of the same length. The involvement of certain groups of muscles cannot be explained by changes in the muscles per se, or the length of axones innervating such muscles. This selection for certain groups of muscles in tetanus intoxication must depend upon a central mechanism, and not on a peripheral one.

We know that tumours of supra-nuclear centres, especially cerebellar tumours, produce a tonus distribution /

distribution very similar to that of general tetanus. HUGHLINGS JACKSON (11, 12) was the first who drew attention to this analogy by speaking of tetanus-like seizures in cases with cerebellar tumours. Experimentally one can produce a distribution of rigidity similar to that of general tetanus, for instance in the decerebrate rigidity one finds an increase of tonus in the extensors of the limbs, trunk, neck and masseter.

SHERRINGTON (22) also, who investigated decerebrate rigidity drew attention to the similarity between tetanus rigidity and decerebrate rigidity. SHERRINGTON writes, "Strychnine and tetanus toxin administered to an animal in decerebrate rigidity increase that rigidity. The posture assumed by the limbs, neck, tail, head etc. in strychnine poisoning and in tetanus resembles closely in many respects the attitude of decerebrate rigidity. There are differences - for instance, the ankle is often rigidly extended in tetanus, whereas it is little affected in decerebrate rigidity; nevertheless there is much general resemblance."

These facts suggest that the mechanism of tetanus rigidity is not only dependent on the spinal cord but also on the higher centres.

The /

The object of this work was to analyse the influence of the higher centres on the spinal cord on the production of such a distribution of rigidity in tetanus intoxication. To that end equal doses of tetanus toxin were injected at corresponding places into the hind legs of rats, cats and dogs (the minimum lethal dose of toxin used in these experiments was, for a mouse of 10 grams weight, 0.01 mg.). At varying periods before injections, spinal and supraspinal centres of one or both sides were removed in an attempt to influence the distribution of the rigidity in tetanus intoxication. Before starting these experiments it was necessary experimentally to exclude:-

First: whether the place of injection of the toxin into the hind limbs has any influence on the distribution of rigidity in local tetanus.

Second: whether an altered position of the limbs would influence the distribution in cases where the central nervous system had not been interfered with.

GROUP I A.

Tetanus toxin was injected into different areas of the hind legs in rats.

RAT I. January 3. 1924 injected subcutaneously 0.1 /

0.1 mg. of tetanus toxin in the neighbourhood of the right gastrocnemius.

January 6. 1924 rigidity developed in the right hind leg which was held in extension, all three joints being equally affected.

RAT II. January 3. 1924 injected subcutaneously 0.1 mg. tetanus toxin in the neighbourhood of the knee-extensors on the right side.

January 6. 1924 local tetanus of the right hind leg developed, the limb being held in extension, and all three joints being equally affected.

RAT IV. January 4. 1924 injected subcutaneously 0.25 mg. of tetanus toxin in the neighbourhood of the flexors of the hind leg.

January 6. 1924 extensor stiffness of the hind leg of injected side appeared. The animal died on 14th January 1924.

RAT VIII. January 8. 1924 injected subcutaneously of tetanus toxin 0.5 mg. into the flexor of the ankle. On the 10th January 1924 stiffness appeared in the extensor of the ankle. On the 11th January 1924 extensor stiffness of the whole limb and rigidity of the trunk muscles started on the homo-lateral side. Animal died the same night.

From these experiments it was concluded that the place /

place of injection has no influence on the distribution of the rigidity. The rigidity invariably occurs in the extensors whether the toxin was injected into the extensor or flexor muscles.

In all experiments detailed below injections were made in the gastrocnemius or in its neighbourhood.

GROUP I B.

An attempt has now been made to change the distribution of the rigidity in tetanus intoxication by mere fixation of the hind leg in a flexed position before and after the injection of tetanus toxin. These experiments have given such uniform results that only one case will be cited.

RAT VII. January 6. 1924 right hind leg was fixed in plaster of Paris, all joints being in a position of flexion.

January 8. 1924 plaster of Paris taken off and an injection of 0.5 mg. tetanus toxin given. The injection was made into the gastrocnemius of the limb. Immediately after the injection the limb was again fixed in a flexed position.

January 10. 1924 this second plaster case was removed. Stiffness was noticed in the leg. The limb was flexed at the knee to an angle of 45 degrees. Stiffness was well marked at the ankle and at the knee. Within /

Within a few hours the same limb gradually assumed a more extended position, until finally the position of the limb differed in no way from that of the limb of an animal whose leg had not been fixed in a definite position during the development of tetanus rigidity.

Thus it is not possible to change the distribution of tetanus rigidity by the fixation of limbs in positions which would favour flexor rigidity, even though such fixations be made several days before the injection of tetanus toxin, and again later.

GROUP II.

This group of experiments was carried out to determine the influence of supraspinal centres on the development of tetanus rigidity. GUMPRECHT (8) found that injections of Bouillon culture of tetanus toxin into the right leg of a guinea-pig several days after total section of the spinal cord, produced extensor stiffness of that leg. Experiments which he performed on mice, in which section of the spinal cord was made just after tetanus rigidity had developed, destroyed such rigidity, but several hours after operation spasms returned, and with the spasms extensor rigidity again appeared. From these experiments he concluded that tetanus rigidity is not influenced by section of the spinal cord, or if influenced, then only /

only in such a way as to make the cramps less frequent and the contractions less rigid, owing to a loss of part of the sensory impulses.

Experiments, in which total sections of the spinal cord are made, can only prove that the supra-spinal centres are not necessary for the development of the rigidity, but they cannot show whether the supra-spinal centres have or have not an influence on the development of the rigidity.

To answer this question experiments of hemisections of the cord are necessary. Immediately after hemi-section, as well as several days after this operation, injection of tetanus toxin must be given.

In some experiments the injections were given into both hind legs, and in others only into the hind leg of the operated side.

A. Hemisection.

RAT 14. January 14. 1924 hemisection of the spinal cord on the right side at the level of the last rib was performed. Immediately after operation 0.25 mg. of tetanus toxin was injected into each hind leg. On January 15. 1924 the rat could move both hind legs, but the movement in the right leg was impaired.

January 16. 1924 beginning stiffness of both gastrocnemii, but the stiffness was not so marked in the /

the right gastrocnemius as in the left. It was easier to flex the ankle by passive movement on the right side. The rat died during the night of the 17th.

RAT 15. January 23. 1924 hemisection of the right side at the level of the last rib. Two hours after operation the muscles controlling the ankle and the knee were paralysed, but at the hip active flexion was still possible. In the afternoon tetanus toxin 0.25 mg. was injected into each hind leg.

January 25. 1924. In the morning of the 25th extensor stiffness was noticed in the left leg; no stiffness in paralysed leg; lateral flexion of the trunk to the left, and rigidity of the left trunk muscles were noticed.

On the evening of the 25th slight stiffness was noticed in the paralysed limb, but there was a definite difference in degree on the two sides. It was much easier by passive movement to flex the ankle on the right, i.e. paralysed side, than on the left. Animal found dead on the morning of the 26th.

CAT 17. January 24. 1924 hemisection of spinal cord on the left side at the level of the last rib was performed. Paresis of the left hind leg resulted. No impairment of movement on the right side.

January 29. 1924 weak movements occurred in the left /

left leg, especially marked at the hip.

January 29. 1924 2.5 mg. tetanus toxin was injected into each hind leg.

January 31. 1924 extensor stiffness in all 3 joints of the right leg was observed. The left leg also showed extensor stiffness at the ankle, but this was not so well marked as on the right side.

The left knee and especially the left hip were held in a position of almost rectangular flexion. The difference between the positions of the hind legs was best seen when the cat was held supported by its tail.

February 1. 1924 the stiffness on the left side was more marked. The hip and knee were held in an obtuse angle, and the ankle was nearly in extension. The stiffness was much weaker on the left side than on the right.

B. Total Sections.

A series of experiments were also carried out to study the influence of total section of the spinal cord on the development of tetanus rigidity.

RAT 20. January 7. 1924 a total section of the cord in the dorsal region was performed. Immediately after operation 0.25 mg. tetanus toxin was injected into each hind leg.

At /

At no time did rigidity develop, but the animal died on the 12th January 1924.

CAT 37. April 1. 1924 total section of the spinal cord at the level of the last rib was performed. This resulted in total paresis of both hind legs.

April 6. 1924 2.5 mg. of tetanus toxin was injected into both hind legs.

April 8. 1924 onset of extensor stiffness in the hind legs, which was more marked at the ankles.

April 9. 1924 extensor stiffness was now more marked, but passive movements were possible at the knees; the hips however were quite flexible.

Summary of CAT 37. The degree of stiffness was much less marked in this animal than in animals where tetanus toxin was injected without section of the spinal cord.

By these experiments we are convinced that the supra-spinal centres must have an influence on the development of the rigidity in local tetanus. The stiffness did occur in the paralysed limb, but it was not so well marked as in the limb of a normal animal. This was more striking after hemi-section, where it was possible to make a comparison between the normal and /

and the paralysed side. This difference was most marked in animals who received the toxin injections immediately after operation, and in which the toxin reached the anterior horns of the spinal cord at the time when the limbs were totally paralysed.

An objection could be raised that the shock of the operation on the spinal cord prevented the development of rigidity in these experiments. But even in cases where the onset of rigidity was a week after the operation, the stiffness was only less marked in operated, as compared with non-operated, animals.

From the above experiments we now conclude that section of the spinal cord produced a lower degree of rigidity in tetanus intoxication owing to the cutting off of the permanent flow of innervation, which is exercised by the supraspinal centres on the spinal cord; these centres have an important influence on the development of local tetanus.

A second objection which can be raised is that section of the spinal cord after the full development of rigidity does not alter the degree of stiffness. It can be said in answer, however, that in such cases the stiffness is not only maintained by the central nervous system, but also by a secondary change in the rigid muscles themselves.

FRÖHLICH & MEYER (7) have shown that section of the peripheral nerves, made some days after the onset of rigidity, does not alter that rigidity, and they stated that such a rigidity was the result of secondary change in the rigid muscles.

By the next experiment it is shown that such a change was the cause of the non-efficacy of section of the spinal cord after the full development of tetanus rigidity. In a cat (experiment CAT 28 of group III) the right motor centre of the hind leg was destroyed. 2.5 mg. of tetanus toxin was injected into each hind leg. Two days later extensor stiffness developed in both hind legs. Four days after operation when the extensor stiffness was fully developed in both hind legs, section of the spinal cord was performed. This section was not followed by any alteration in the position, or in the degree of rigidity of the hind legs. On the 5th day after the original operation, the sciatic nerve was cut. This did not have any influence on the stiffness which remained unaltered until the animal was killed.

GROUP III. CORTICAL DESTRUCTIONS.

In the next series of experiments, unilateral cortical and sub-cortical centres of the fore-brain were destroyed.

After /

After operation equal doses of tetanus toxin were injected into the calf muscle of each side.

The accuracy of the surgical destruction of the various centres was controlled post-mortem - macroscopically, and in some cases, microscopically. Serial sections of the whole area involved were made and stained with Haemalaun-Eosin and Methylene Blue after Nissl.

In the first set of experiments cortical centres were attacked.

RAT 20. January 29. 1924 the skull over the right cortex was opened and the superficial cortex of the right side was destroyed. 0.25 mg. tetanus toxin was injected into each hind leg. On February 1. 1924 extensor stiffness in both hind legs was noticed.

On February 2. 1924 there was well-marked extensor stiffness in both hind legs. The animal now adopted a scoliotic attitude with concavity to the right. The tail was laterally curved with concavity to the left. On the evening of the 2nd the animal developed generalised muscular spasms and died the same night.

The post-mortem showed a bulging at the side of the destroyed cortical area. The destruction extended over practically the entire dorsal and dorso lateral /

lateral surfaces of the right hemisphere, only a strip of cortex near the middle line and the occipital hemisphere remaining intact.

Microscopical examination of the protruding area showed the white substance of the Internal Capsule and the Corpus Callosum infiltrated with inflammatory cells and haemorrhage. This infiltration extended down as far as the superficial part of the Caudate Nucleus and of the Putamen.

In the hind part of the brain the Cornu Ammonis was destroyed by haemorrhage, and it also formed part of the herniation. The lateral ventricle was found to be opened.

Summary of CASE 20. In this experiment in which we have destruction of practically the entire cortex, and in which the deeper ganglia had been involved (only in the superficial parts), no alteration in the usual development of stiffness resulted, except scoliosis of the trunk and curvature of the tail.

CASE 24 RAT. On February 11. 1924 the cortex on the right side was destroyed. Immediately after operation 0.25 mg. of tetanus toxin was injected into each hind leg.

On February 13. 1924 extensor stiffness of both hind legs and of the trunk muscles developed (see Fig.

2 & 3.) The animal died during the night of the 14th.



Fig. 2.



Fig. 3.

The post-mortem showed bulging at the side of the destroyed cortex. Macroscopically, it showed destruction of the dorsal part of the lateral surface of /

of the cortex (Fig. 4 & 5.) Microscopically,

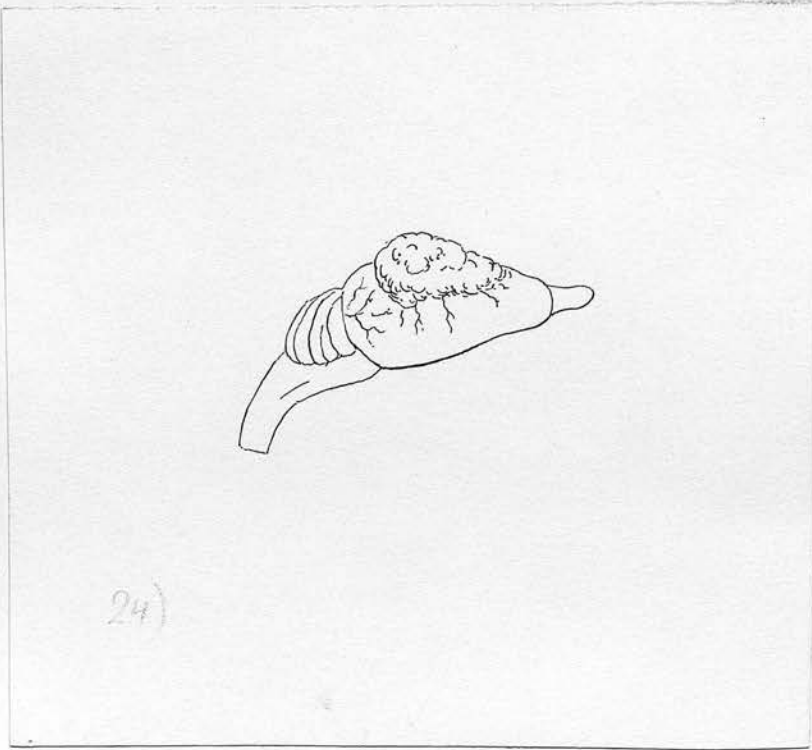


Fig. 4.

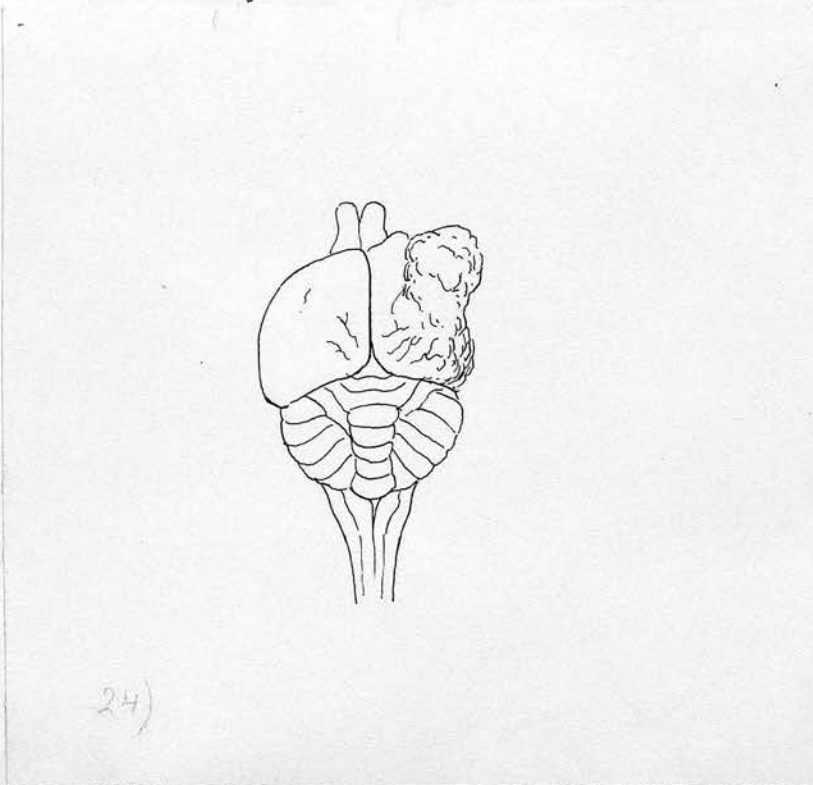


Fig. 5

sections showed destruction of the cortex without involvement of the white substance.

Summary. Destruction of the cortex alone had no influence on the development of rigidity.

CAT 28. February 14. 1924 the right leg area on the cortex was localised by means of an electric battery and destroyed. Immediately after operation 2.5 mg. of tetanus toxin was injected into each hind leg.

February 16. 1924 extensor stiffness developed.

February 18. 1924 extensor stiffness was now well developed (Fig. 6), hence this animal was used

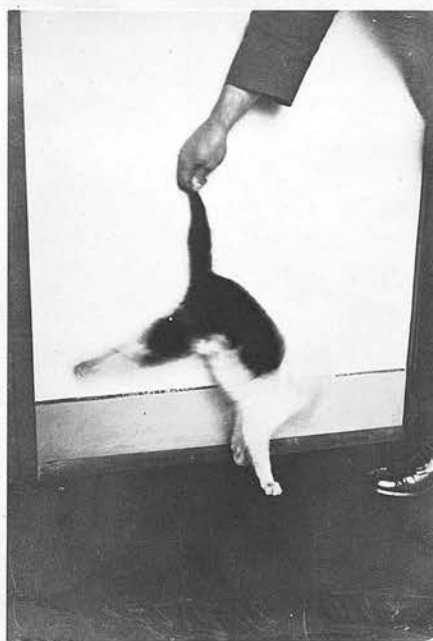


Fig. 6.

for section of the spinal cord (see page 17).

At /

At post-mortem it was seen that the destruction of the cortex was just behind the sulcus cruciatus of the right side. The anterior parts of the gyrus coronalis and gyrus ecto-sylvius were also a little involved.

Summary. The destruction of the motor zone in this animal had no influence on the development of the rigidity in local tetanus.

Summary of cortical lesions. Having studied the above cases, we conclude that the destruction of the cortical centres in the examined animals (cats and rats), and of the fibres starting from the cortical motor centres, plays no part in the development of tetanus rigidity. Local tetanus in animals, after destruction of the cortical layers, dorsal and lateral to the deeper ganglia, develops in the same way as that which was seen in non-operated animals. In some of the cases one notices asymmetry of the position of the tail and trunk. The asymmetry of the tail is also seen in normal rats (see Fig. 1). The asymmetry of the trunk, which was seen in Case 20, was explained by the microscopical examination, which showed some involvement of the superficial structure of the deeper ganglia (Putamen and Nucleus Caudatus), which have, as will be seen in the next series /

series of experiments, an influence on the distribution of the rigidity in tetanus.

GROUP IV.

In this series unilateral destruction of the deeper ganglia of the fore-brain (that is, corpus striatum) was made before the bi-lateral injections of tetanus toxin were given. It is not possible to destroy the deeper ganglia without destruction of the covering cortex, but there appeared to be no objection to the making of a combined destruction of cortex and deeper ganglia, as we have seen in the above series of experiments that the destruction of the cortex and its fibres have no influence on the development of the rigidity. The method adopted for the destruction of the Striatum was by means of Aspiration. This had been the method used by BAGINSKY and LEHMANN (1).

Aspiration was effected by suction of brain substance through a fine drawn vacuum glass tube, this method being quite successful in obviating haemorrhage. For the destruction of the Caudate Nucleus in cats the aspiration method could not be employed; an instrument similar to that described by SCHÜLLER (20) being used instead. This instrument consists of a fine metallic tube, enclosing a wire brush. This metallic tube is inserted to the required depth, and then, /

then, with the brush held in position, the tube is withdrawn. The brush is then rotated, causing destruction of the desired nucleus. The brush is then again drawn up into the tube and the tube withdrawn without great destruction of the cortex.

For destruction of the Corpus Striatum in cats it is necessary to penetrate the cortex at a point 15 mm. lateral from the middle line, and 9 mm. behind the Sulcus Cruciatus. The instrument is then held vertical to the surface of the cortex, and pushed in for a distance of 15 mm. The tube is then withdrawn for 5 mm. leaving the brush behind. The brush is then rotated, and the required area is destroyed.

RAT 18. This animal was intended for a case of cortical destruction. The anatomical examination showed that the destruction penetrated deeper than was originally intended, therefore this experiment was classed as a case of nuclear destruction.

On January 28. 1924 the skull was opened and the right cortex was removed. January 29. 1924 0.25 mg. tetanus toxin was injected into each hind leg.

January 31. 1924 both hind legs were held at the hip and the knee in obtuse angle, the ankles were held at an angle of 90 degrees; the toes of both hind legs were held in flexion. In the afternoon of January 31. /

31. 1924 the animal developed spasms. The flexor stiffness was more marked on the right side. Animal died the same night.

Anatomical examination. The dorsal and lateral surfaces of the right cortex were destroyed, leaving a thin strip of cortex in the frontal and occipital poles and along the mid-line.

In a series of sections it was seen that the Caudate Nucleus was bulging into the area of cortical extirpation, and that it was itself partially destroyed, especially on the dorso-lateral side. Furthermore there was a haemorrhage into the medio-ventral side of the caudate nucleus near the lateral ventricle (Fig. 7).

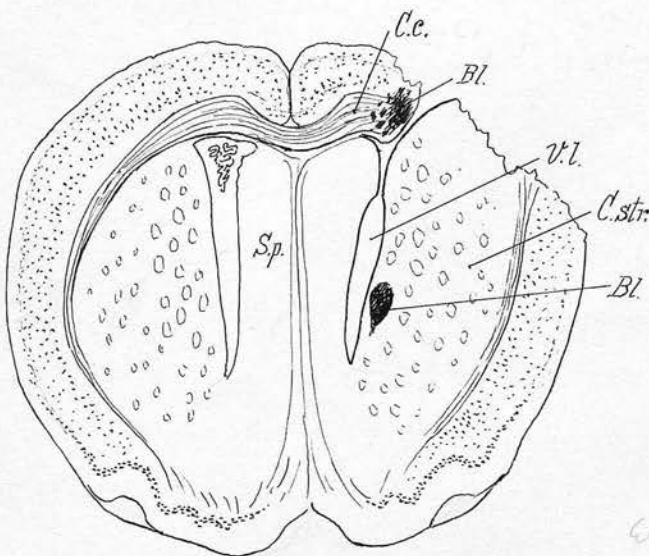


Fig. 7.

Summary of RAT 18. Destruction of the dorso-lateral surface of the right cortex with a lesion of the dorso-lateral part of the caudate nucleus of the same side, and with a little haemorrhage into the medial part, produced a new phenomenon.

With such a lesion we could observe a definite alteration in the development of tetanus rigidity. Instead of the extensor rigidity there was now the tendency to flexor rigidity in both hind legs. This was more marked on the homo-lateral side, where it showed marked flexion of the ankles and toes.

RAT 21. February 5. 1924. We destroyed the dorso-lateral surface of the cortex, opened the lateral ventricle and destroyed the right Caudate Nucleus by aspiration. Immediately after aspiration 0.25 mg. of tetanus toxin was injected into each hind leg.

February 7. 1924 the left hind leg was held in an obtuse angle at the hip, knee and at the ankle; the toes were held in partial extension. The right leg was flexed at all joints. The hip and knee were held at an obtuse, and the ankle at a right angle, the toes /

toes well flexed (Fig. 8). All the flexed joints re-

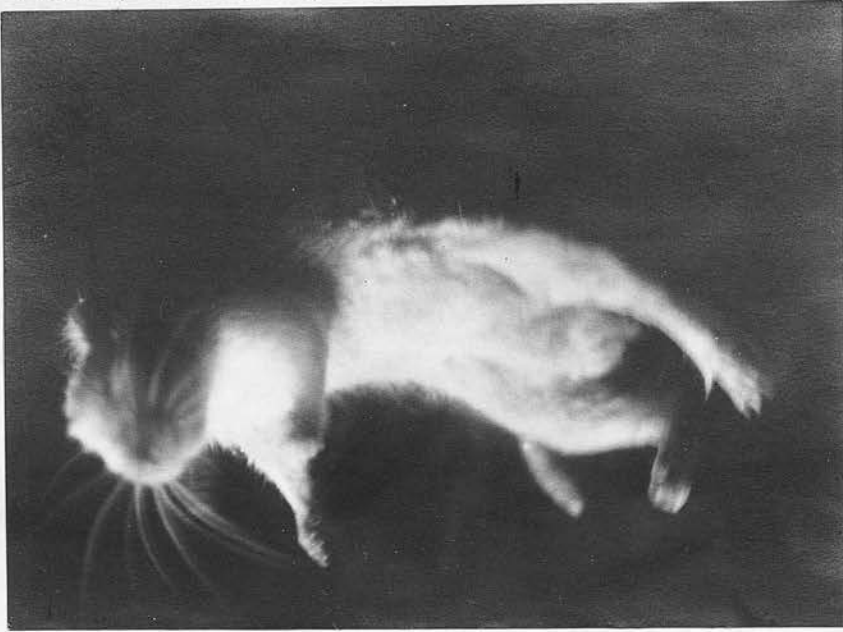


Fig. 8.

sisted extension. A true flexor rigidity existed on the right side. The trunk was kyphotic and scoliotic, with concavity to the right side. Animal died on the morning of the 8th.

Anatomical examination. The lateral surface of the cortex was ablated (Fig. 9 & 10). On serial

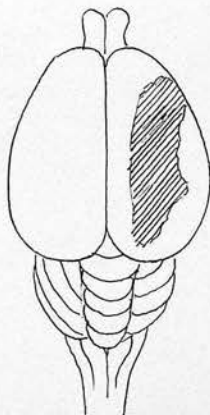


Fig. 9.

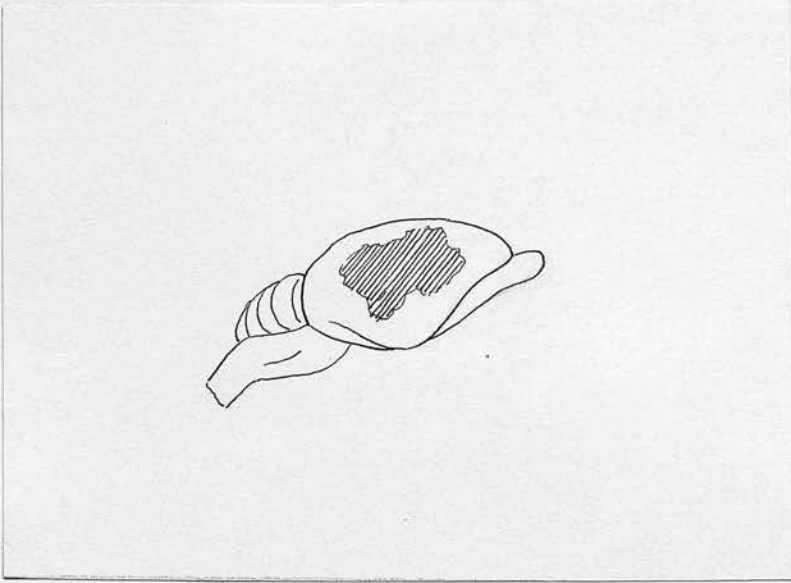


Fig. 10.

sections the striatum was destroyed with the exception of a small medial portion (Fig. 11). Sections

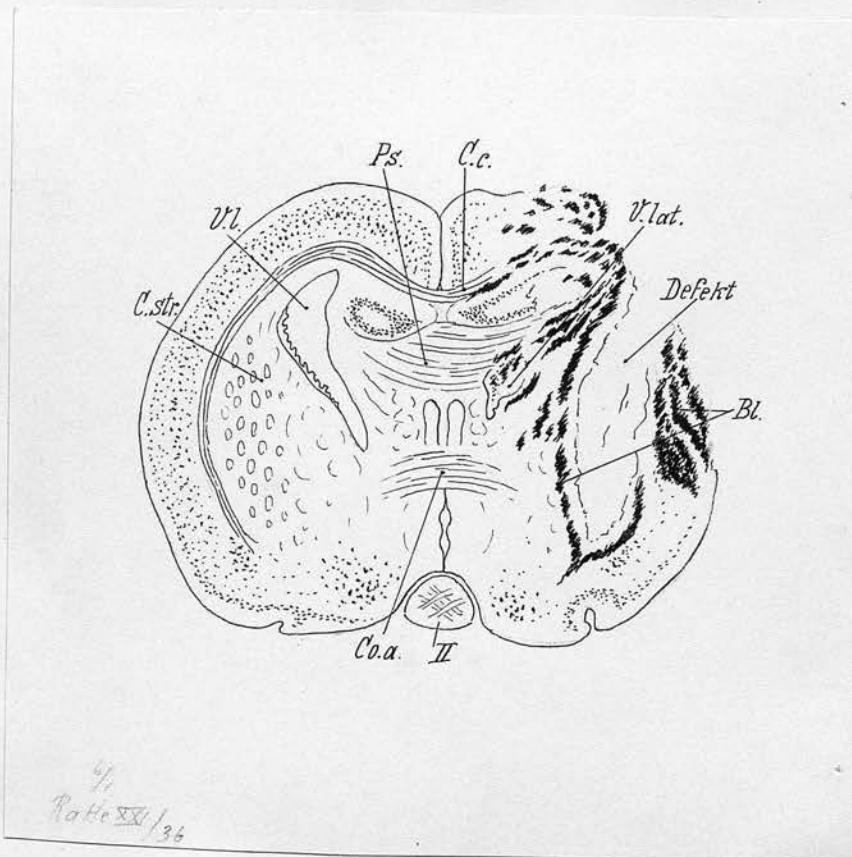


Fig. 11.

of the hind parts (Fig. 12) showed infiltration and

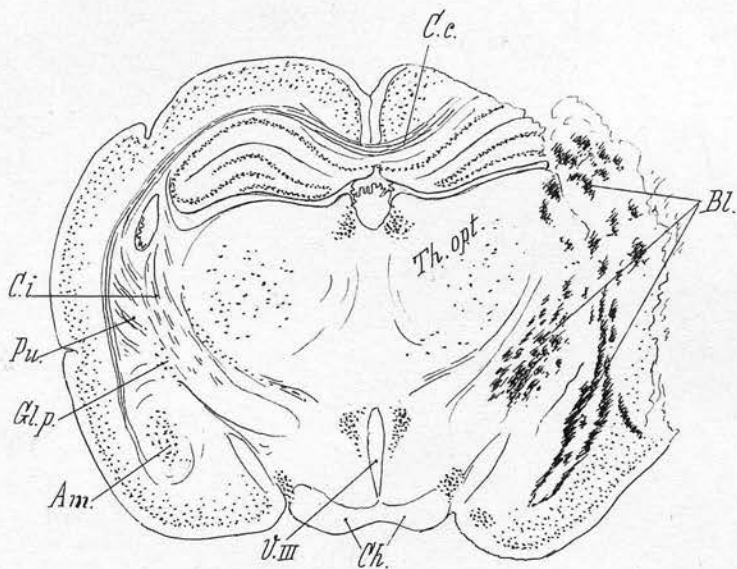


Fig. 12.

haemorrhage into the caudal part of the Putamen, Globus Pallidus, Amygdala, and the Internal Capsule. The Optic Thalamus was not involved.

Summary of RAT 21. Almost complete destruction of the Striatum with ablation of the covering cortex completely changed the type of rigidity, especially on the ankle of the homo-lateral side, from extensor rigidity to flexor rigidity.

CAT /

CAT 31. February 26. 1924 Corpus Striatum was destroyed on the right side by the tube and brush method. Brain herniated immediately after operation. In the afternoon the animal made "manège movements" to the left side, i.e. reverse to hands of watch. 2.5 mg. tetanus toxin was injected into each hind leg the same afternoon.

February 27. 1924 left hind leg showed clumsy movements - impaired function. When the animal was held with the hind legs hanging, the right hind leg was pulled up more deliberately than the left. No more manège movements were seen.

February 28. 1924 some stiffness in both hind legs was noticed.

March 1. 1924 distinct flexor stiffness was now developed in both hind legs, especially the right. The knee was held in obtuse, and the ankle of the right hind leg was held nearly at a right angle (Fig. 13).

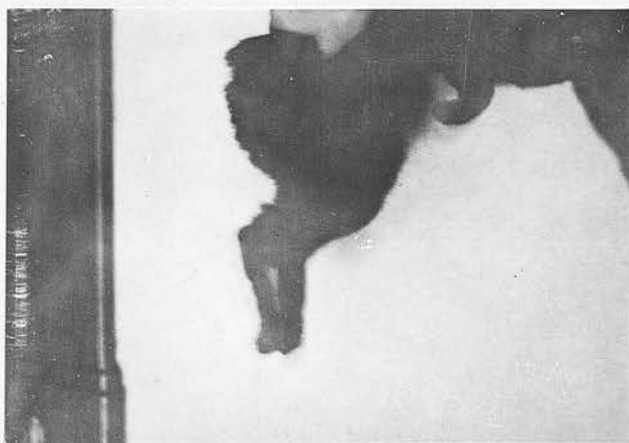


Fig. 13.

On making passive movements, or attempting to extend the flexed joints, one met with marked resistance. By flexing the ankle and knee from a right angle to an acute position one also met with resistance, but this resistance was not so strong as by manipulation in the opposite direction.

Anatomical examination. We observed herniation of the right cortex in the anterior part of the gyrus coronalis and ecto-sylvius anterior. Sections showed that the haemorrhage, starting from the herniated cortex, extended through the white substance into the lateral ventricle, destroying the head of the Caudate Nucleus, and also involving the dorsal part of the Septum pellucidum. The haemorrhage also extended caudally, involving the dorsal part of the Putamen and the Globus Pallidus, and the Nucleus Lateralis of the Optic Thalamus and the Internal Capsule between them.

Summary of CAT 31. A destruction of the Corpus Striatum and the Gyrii Coronalis and ecto-sylvius anterior, fibres of the Capsula Interna and the dorsal part of the Nucleus Lateralis of the Optic Thalamus caused flexor rigidity which was especially marked on the homo-lateral side.

CAT 33. On March 7. 1924 with the same method as /

as Case 31 the deep ganglia of the right side were destroyed. No manège movements, no weakness, no sure change in tone were noticed after operation.

March 14. 1924. Seven days after operation 2.5 mg. tetanus toxin was injected into each hind leg.

March 17. 1924. We noticed flexor rigidity of both hind legs. The knee and hip were held in a right angle position. The ankle was held in an obtuse angle position. The right leg, however, was more flexed than the left, and the toes on the right side were also flexed.

March 18. 1924. The animal had general tetanus. The trunk was kyphotic and the fore-legs were also held in a flexed attitude. Animal died on the 18th.

Anatomical examination of CAT 33. The gyrii coronalis and ecto-sylvius anterior were prolapsed. On sections the path of destruction traversed the capsula interna. It extended from the cortex to the dorso-lateral part of caudate nucleus and the dorsal part of the Putamen. The tail of the caudate nucleus and the dorso-lateral part of the optic thalamus were also involved.

Summary of CAT 33. Here, as in the previous case, the destruction of the striatum resulted in flexor rigidity, although the lesion was made a week before /

before injection of tetanus toxin and 10 days before the development of stiffness. No gross motor change took place after the operation; even though there was involvement of fibres of the internal capsule and the dorso-lateral part of the optic thalamus.

The following experiment, CAT 30, was performed to determine whether the destruction and herniation of the cortex at the point where the tube was introduced, had any effect on the tetanus rigidity.

CAT 30. February 23, 1924 the gyrii coronalis and ecto-sylvius anterior were destroyed.

February 28, 1924 1.8 mg. of tetanus toxin was injected into each hind leg.

March 1, 1924 stiffness beginning.

March 3, 1924 there was now well marked extensor stiffness in both hind legs. This remained until the animal was killed on the 8th.

The anatomical examination showed herniation of the destroyed area, i.e. the gyrus coronalis and gyrus ecto-sylvius anterior.

Summary. Destruction of the cortex at the place where the tube was introduced for destruction of deeper ganglia had no influence on the development of the rigidity.

CAT 32. The following experiment, undertaken to further /

further determine the effect of destruction of the deeper nuclei by means of the tube and brush method, failed to destroy the caudate nucleus and therefore it was used to show the effect of destruction of nuclei and fibres surrounding the caudate nucleus.

February 26. 1924 after the cortex had been exposed the tube for destruction by accident was directed in a slanting direction, but otherwise the procedure was the same as previously described for destruction of the caudate nucleus.

February 26. 1924, p.m. 2.5 mg. of tetanus toxin was injected into each hind leg.

February 27. 1924. Weakness and clumsiness were observed, especially in the left hind leg. This condition was more marked than in CAT 31, when it was held with the hind legs hanging.

February 28. 1924. Well marked extensor stiffness, with no differences, was observed. This stiffness continued until the animal was killed on the 9th.

Anatomical examination showed herniation in the region of the gyrus coronalis, sigmoideus posterior and part of gyrus ecto-sylvius anterior. On section the head of the caudate nucleus was seen to be intact. The part of destruction extended to the tail of the caudate nucleus, involving by haemorrhage the tail of the /

the caudate nucleus and the lateral nucleus of the optic thalamus. The right portion of the corpus callosum and the fibres of the internal capsule in the neighbourhood of the caudate nucleus were also involved in the destruction.

Summary. A big destruction of the cortex, as in Case 31, with destruction of the right side of the corpus callosum, dorso-lateral part of thalamus, tail of the caudate nucleus, and involvement of fibres of the internal capsule, but without involvement of the head of the caudate nucleus, had no influence on the development of the rigidity.

Final Summary of GROUP IV.

Experiments on rats and cats have shown that destruction of the corpus striatum, especially the head of the caudate nucleus, preceding tetanus toxin injections, has an influence on the development of the rigidity. In animals, where these parts have been destroyed, the normal extensor rigidity did not develop, but the stiffness resulted in flexor rigidity, especially on the homo-lateral side.

By experiments of Group II (destruction of the cortex covering the corpus striatum, and especially of the motor zone), and also by the control experiments /

experiments of Group IV, it was shown that the destruction of the cortex and its fibres, as also of the dorso-lateral part of the thalamus in the neighbourhood of the caudate nucleus, did not change the type of rigidity.

One must conclude that destruction of the head of the caudate nucleus changes the type of rigidity.

GROUP V. CEREBELLAR EXTIRPATION.

The experiments were made on rats, rabbits and dogs. The right side of the cerebellum was extirpated before the injections of tetanus toxin. The extirpations on rats and rabbits were made by the method of aspiration, as has been described. The skull over the cerebellum was opened by removal of the occipital bone.

In dogs, however, it was not possible to aspirate the cerebellum, so it was destroyed after the method of DUSSE de BARENNE (6). The occipital bone was cleared and trephined, the dura incised, and the cisterna sub-cerebellaris was opened by removal of the arachnoid. The cerebellum was now lifted up by means of a spatula, so that the hind part of the fourth ventricle could be seen.

With a small knife a section of the vermis was made in the middle line. A suitable spatula was introduced /

introduced between the petrous portion of the temporal bone and the cerebellum. The lateral part of the cerebellum was lifted and a section was made from ventro-lateral to medio-dorsal. The portion of the cerebellum above the section was taken away.

RAT 34. February 27. 1924 the right half of cerebellum was aspirated. After operation 0.25 mg. tetanus toxin was injected into each hind leg. In the afternoon the animal showed scoliosis of the trunk with concavity to the right side, and rolled to the same side.

The afternoon of February 28. 1924 extensor stiffness was noticed in both hind legs, the stiffness, however, did not develop to the same degree on the right as compared to the left. It was much easier to get flexion by passive movement on the right side. Animal died on the morning of 29th.

CASE 35 DOG. March 17. 1924 right half of the cerebellum was removed. Immediately after operation 5 mg. of tetanus toxin was injected into each hind leg. The afternoon of March 17. 1924 the animal was lying on its right side. When holding animal by skin of his back one could see there was a tendency of the trunk to flexion with concavity to the right side. On the subsequent days the animal remained in the same condition. /

condition.

March 21. 1924 symptoms of tetanus manifest. The stiffness was more marked in the left hind leg as compared to the right, but both showed extensor rigidity. The animal very soon developed general tetanus with attacks of spasms which were also seen in the front legs.

March 23. 1924. Symptoms of general tetanus were noticed. Animal died the same day. After death one noticed that the limbs on the right side had not the same degree of rigidity as on the left.

Anatomical Examination. The right half of the cerebellum was almost totally destroyed, except the flocculus.

Summary of cerebellar experiments. In these experiments it was seen that extirpation of one half of cerebellum did not prevent the development of extensor rigidity in both hind legs. The stiffness of the rigid muscles was not so well marked on the side of operation. We must conclude that the permanent innervation exercised on the spinal cord from the cerebellum plays a rôle in the development of extensor rigidity. The cerebellar innervation helps to increase the degree of extensor rigidity. The posture, however, adopted by the limbs in tetanus intoxication develops /

develops independently of the influence of cerebellar origin. One objection one could raise is, that in these experiments the rigidity is developed during the time of excitation symptoms of cerebellar extirpation (i.e. rolling movements in rats, curving of trunk to homo-lateral side in dogs).

If the excitation symptoms had an influence on the rigidity, then one would expect an increase of tonus on the side of operation and not a lower degree, as was noticed. The difference in rigidity in the hind legs in these experiments must be a sign of loss of cerebellar function and not of excitation.

FINAL CONCLUSION AND SUMMARY.

The primary purpose of this work was to determine, if possible, the influence supra-spinal centres have upon the development of rigidity in tetanus intoxication, and to analyse this influence. After undertaking this work, our observations especially directed our attention to the function of the corpus striatum. This final conclusion not only deals with the influence of supra-spinal centres on tetanus rigidity, but also with the deduction that the corpus striatum normally has a function of regulating the distribution of /

of muscle tonus which is necessary for the normal position of the body.

In normal tetanus rigidity, one notices stiffness of the extensors of the limbs, trunk, and neck. These are the muscles which act against gravity, as SHERRINGTON (22) has stated, and which, in normal life, have a higher tonus than the flexors. Tetanus rigidity is only an exaggeration of the normal tonus of the body, the same as decerebrate rigidity after section through the midbrain.

By exaggeration of tonus, as a result of tetanus intoxication, one hoped to find differences in tonus distribution after extirpation of such supra-nuclear centres, which in an unintoxicated animal have no sure influence on muscle tonus. In this way it seemed possible, not only to analyse the influence of supra-nuclear centres in tetanus rigidity, but also to get a better idea of the normal functions of the different centres. The importance of these supra-spinal centres in the pathogenesis of tetanus rigidity has been shown by that group of experiments where a hemisection of the cord preceding the injection of the same quantity of tetanus toxin into the two hind legs produced a distinct lower tonus on the operated side.

Experiments in cerebellar extirpation show that after /

after hemi-extirpation of the cerebellum the degree of tetanus rigidity is lower on the homo-lateral side, but that the normal distribution and, therefore, the type of that rigidity, is not interfered with.

EDINGER, who studied the anatomical relations, concluded in accordance with the experiments of LUCIANI that the cerebellum is the centre for statotonus, i.e. that the cerebellum exercises the innervations which are necessary for the normal tension of the muscles, which gives to the body the normal posture against gravity. The theory of EDINGER was questioned by the experiments of MAGNUS and DE KLEYN who found that a great group of tonic reflexes, which are necessary for the normal posture of the body, i.e. labyrinth reflexes and neck reflexes, remained after total extirpation of the cerebellum.

We must not forget that the tension of the striated muscles is not only influenced by the labyrinth and neck reflexes, but that the proprioceptive impulses starting in the limbs themselves have a great influence on muscle tonus. It has been demonstrated that the proprioceptive reflexes starting from the limbs are partly dependent on the cerebellum (SPIEGEL) (23).

From the above statements we conclude that the cerebellum /

cerebellum is not the only centre for stato-tonus, but it merely has some influence on the maintenance of posture. This conclusion is in accordance with our results - tetanus intoxication where hemi-section of the cerebellum did not alter the usual type of rigidity, but only resulted in a lower degree of stiffness.

Extirpation of the motor zone of the cortex had no influence on the form or degree of rigidity in tetanus intoxication. Subcortical lesions resulted in marked differences in groups of muscles involved and positions adopted by the limbs. In cases of combined lesions of sub-cortical ganglia, with injections of tetanus toxin local tetanus took the form of flexor rigidity instead of extensor stiffness. This alteration was most marked on the homo-lateral side.

Further experiments show that the ganglion which brought about such an alteration was the corpus striatum, i.e. the caudate nucleus and the putamen. Destruction of the neighbouring nuclei, i.e. the capsula interna, dorso-lateral part of the optic thalamus, had no influence on the form or degree of rigidity. It is not yet possible to localise more exactly which part of the striatum had the above-described influence. One can state, however, that the /

the destruction of the head of the caudate nucleus had this effect on the rigidity, whereas destruction of the tail of the caudate nucleus had not this effect.

The hind part of the putamen and of the globus pallidus need not necessarily be involved for this alteration, as has been seen in RAT No. 18, where haemorrhage only in the head of the caudate nucleus was found.

Our experiments on the caudate nucleus give, perhaps, also an idea of the normal function of the corpus striatum on tonus regulation, while destruction of the corpus striatum in normal animals give no result, as seen in the literature of previous experimentalists. SCHÜLLER (20), who destroyed the caudate nucleus in dogs, found that all the symptoms observed by the previous authors were caused by destruction of the neighbouring parts, and not by the destruction of the caudate nucleus itself.

He could not find any special symptom after destruction of the caudate nucleus. He also stated that the manège movements, first described by CARLVILLE & DURET which were also observed in certain of our cases, are the consequences of lesions of the internal capsule.

KINNIER WILSON (25), who invented progressive lenticular /

lenticular degeneration with characteristic symptoms of hypertonicity of the skeletal muscles in man, was unable to demonstrate by experiments in apes any evidence that the corpus striatum "exercises any motor functions comparable to that of the motor cortex. There is no evidence that the corpus striatum is a centre for so-called automatic movements. It is electrically inexcitable, and comparatively large unilateral lesions do not give rise to any unmistakable motor phenomena."

KINNIER WILSON (25) also confessed that he had been unable to obtain symptoms similar to hypertonus, as seen in man in cases of lenticular degeneration, in his experiments in apes whose ansa lenticularis had been completely degenerated, or in whose corpus striatum large lesions had been produced. To explain the difference of these observations in man, and the results of his experiments in apes, he states that the functions of the centres of the fore-brain are not identical in man and animals, and that man is much more dependent on his motor cortex than lower animals, and this suggested to him that the function of the corpus striatum differs in different species.

One must not forget, however, that the phylogenetic differences in man and animals are only differences /

differences of degree. When we find that a centre has a special function in man, then there must be expected a similar function of such a centre in animals, but there may be a difference in degree. Inasmuch as the corpus striatum has a similar anatomical structure in man and in animals it can be concluded that the corpus striatum must also influence the muscle tonus in animals.

Our experiments of producing lesions of the corpus striatum, together with the injections of tetanus toxin, demonstrated the influence of the corpus striatum on the tonicity of the skeletal muscles, and manifested itself by the change of local tetanus, which normally has the form of extensor rigidity, to the form of flexor rigidity.

Having seen that the usual extensor rigidity is an exaggeration of the normal tonus distribution between extensors and flexors of the limbs, these experiments, where the destruction of the corpus striatum changed the extensor rigidity into flexor rigidity, suggest that also in normal life the corpus striatum has an influence on the distribution of tonus between flexors and extensors.

PART II.

The Treatment of Tetanus Intoxication.

Various methods for the treatment of tetanus intoxication have at different times been suggested; such as, injections of carbolic acid, magnesium sulphate, tetanus anti-toxin, etc.

Of these methods the only one which proves to be of value is the injection of tetanus anti-toxin. Even this method, however, has its disadvantages. Perhaps the most apparent is that the anti-toxin exerts its full potency only if used before the onset of tetanus symptoms. At the time of development of the symptoms, large quantities of the toxin become fixed in the nerve-cells and the beneficial effect of the anti-toxin is limited to the neutralization of the unfixed toxin.

MEYER & RANSOM (16) demonstrated that the toxin travels along the axones towards the central nervous system and they were successful in preventing the onset of local tetanus by injecting tetanus anti-toxin endoneurally. These experiments were confirmed and extended to man by KÜSTER (13) & CLAIRMONT (5). The disadvantage of this method is that since the toxin is generally distributed throughout the whole body, a method /

method that attacks the diseased only locally, cannot be an efficient one. A better method is the intrathecal injection of tetanus anti-toxin, since in this way the anti-toxin comes in contact with all the motor axones.

The intra-venous and intra-muscular methods can be dismissed in a few words. In both these methods only a small part of the anti-toxin injected reaches the desired destination, i.e. the central nervous system. RANSOM (19).

Several objections have been raised to the intrathecal method. According to RANSOM (18) the anti-toxin is rapidly excreted into the blood; the total quantity injected intrathecally appearing in the blood stream within the space of 24 hours.

This is hardly a legitimate objection as injections are given daily. Another objection that has been raised is that substances injected into the sub-arachnoid space cannot reach the central nervous system since ecto-dermatic tissue is separated from the meso-dermatic tissue by the glia-wall.

Certain observers however maintain that the lymphatic circulation is from the sub-arachnoidal space towards the central nervous system and that in this way substances injected into the sub-arachnoidal space /

space can reach the central nervous system.

Furthermore intra-theccal injections of anti-tetanus toxin aim at neutralization of the toxin in the sub-dural space and not necessarily that in the nervous tissue.

The superiority of the intra-theccal over the intra-muscular method has been strikingly demonstrated by SHERRINGTON, in a series of experiments quoted by BRUCE (4). The experiments were carried out on monkeys - one group of twelve receiving the anti-toxin intra-muscularly and another group of eighteen intra-theccally. All the animals in the first group died, while thirteen in the second group recovered, even though some animals in the second group received smaller doses than any of the animals in the first group. These results clearly demonstrated the superiority of the intra-theccal route according to the method recommended by LEISHMAN & SMALLMAN (14), but the death-rate in this improved method is admittedly still very high, viz. 33%. BRUCE (2, 3).

Under the circumstances further improvement is desirable. Since the cerebro-spinal fluid in tetanus intoxication is rich in tetanus toxin, STINTZING (24) (cited by EISLER & PRIBRAM in Kraus & Levaditi's Handbuch der Technik und Method der Immunitätsforschung, /

Immunitätsforschung, Volume I. 103 - 1908) suggests a new line of attack. How can the toxin be eliminated from the subdural space? The simplest method is by withdrawing the spinal fluid and with it the contained toxin. To assure the further removal of toxin in the subdural space, the tapping of the spinal fluid is combined with intra-theal injections of anti-toxin after a thorough washing out of the sub-dural space with physiological saline. Although this method has been tried in only three cases, the results have proved so successful that it suggests clinical application.

CASE I.

Name. Fanie du Toit.

Age. 17.

Sex. Male.

Admitted to hospital January 28. 1921.

Complaint. Muscular spasms.

Previous History. Measles and whooping cough in childhood, otherwise healthy.

Family History. Healthy.

Present Complaint. Ten days before admission while going about barefooted on a farm, patient received a small laceration on lateral border of left foot over base of 5th metacarpal. The wound being a small one and superficial, no attention was paid to it, and nothing unusual was noticeable.

On the morning of January 27. 1921 patient complained that he was not feeling well; he felt stiffness in the neck and had general body pains.

Towards afternoon stiffness of the jaw set in and patient's medical adviser was consulted. The next morning patient was sent to hospital.

Examination. Well built youth with a pale face, anxious expression and bathed in perspiration. The head was held in an extended position and could not be /



be passively flexed. The eyebrows were drawn up and the conjunctivae somewhat congested. The mouth could not be opened and the masseter muscles were in a state of tonic contraction, with frequent tonic spasms. The muscles of the shoulder and arm were rigid, whereas those of the forearm were flaccid. The long muscles of the back were in a state of tonic contraction with frequent clonic spasms. Permanent arching of the back markedly increased during the clonic contractions, the patient then assuming the opisthotonos attitude.

Abdominal breathing was practically absent, both recti being strongly contracted.

The lower extremities were hyper-extended at the hips and the knees were fully extended.

On the lateral side of base of the 5th left metacarpal was a small wound covered by a septic scab. During the general clonic spasms the extensors of the lower extremities were also thrown into violent contraction, thus causing the patient to assume the typical opisthotonos attitude, i.e. the weight of the body resting on the occiput and the heels. Breathing was rapid and superficial and completely arrested during the clonic spasms.

The lungs were resonant on percussion with a few moist /

moist râles heard at the bases.

The pulse was frequent and soft. No organic cardiac lesion was present. The abdominal organs could not be palpated on account of the rigidity of the muscles.

Patient passed frequent small quantities of urine with a high specific gravity and a trace of albumin.

The bowels were constipated.

Treatment.

Temperature	104.6°	} January 28. 1921.
Pulse	134	
Respiration	46	

Patient is anaesthetised, which stops the clonic spasms, but the general increased tonus remains.

Lumbar puncture is performed in the 3rd lumbar space and 25 cc. of cerebro-spinal fluid withdrawn. An equal quantity of sterilised normal saline is now injected into the subdural space.

The patient is tilted from side to side and up and down, the needle with stilette remaining inserted.

Again 25 cc. are tapped and the above described process repeated six times.

At the end of the 7th tapping 1500 units of anti-tetanic serum is injected intra-muscularly. 3000 units /

units are given into the left buttock.

During the rest of the day the patient receives frequent inhalations of chloroform vapour in order to allay clonic spasms.

January 29. 1921. After receiving a $\frac{1}{4}$ grain of morphia subcutaneously, patient slept well during the night.

The jaw is now less tightly clenched and the clonic spasms greatly diminished in frequency and intensity, the patient still being kept under the influence of morphia.

The temperature has come down to 101.8° ; respiration 38; pulse 126. Patient is roused and given 6 ozs. of milk by means of a feeder. A solution containing 15 grs. each of Chlor. Hyd. and Pot. Bromide, is similarly given.

The bowels are opened by means of a soap and water enema.

January 30. 1921. Under the influence of Chloral Hydrate and Bromide the patient spent a more or less restful night, though more fatigued looking than yesterday. While the tonic spasms remain the same the clonic spasms are gradually subsiding. The milk feeds are continued.

Bowels opened by means of an enema.

Temperature /

Y etams

Notes of Case

Result

[illegible]

4 HOUR CHART.

DISEASE.

Sotanus.

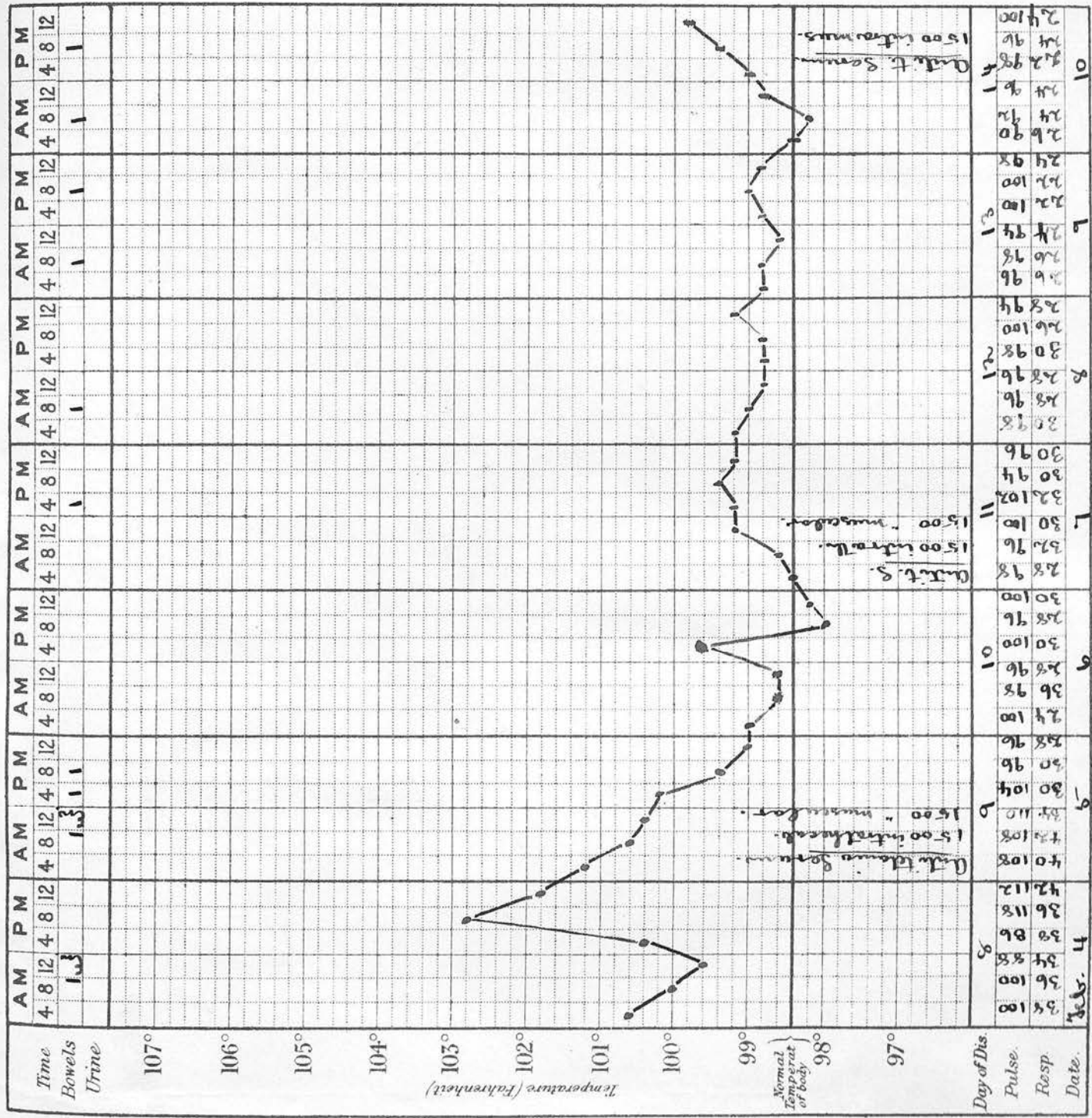
Name { *Marie*
dw Toits

Age *17*

Diet

Case Book No.

Notes of Case



Date of admission

8-1-1921

Result

Name *Jane du Toit*

Age

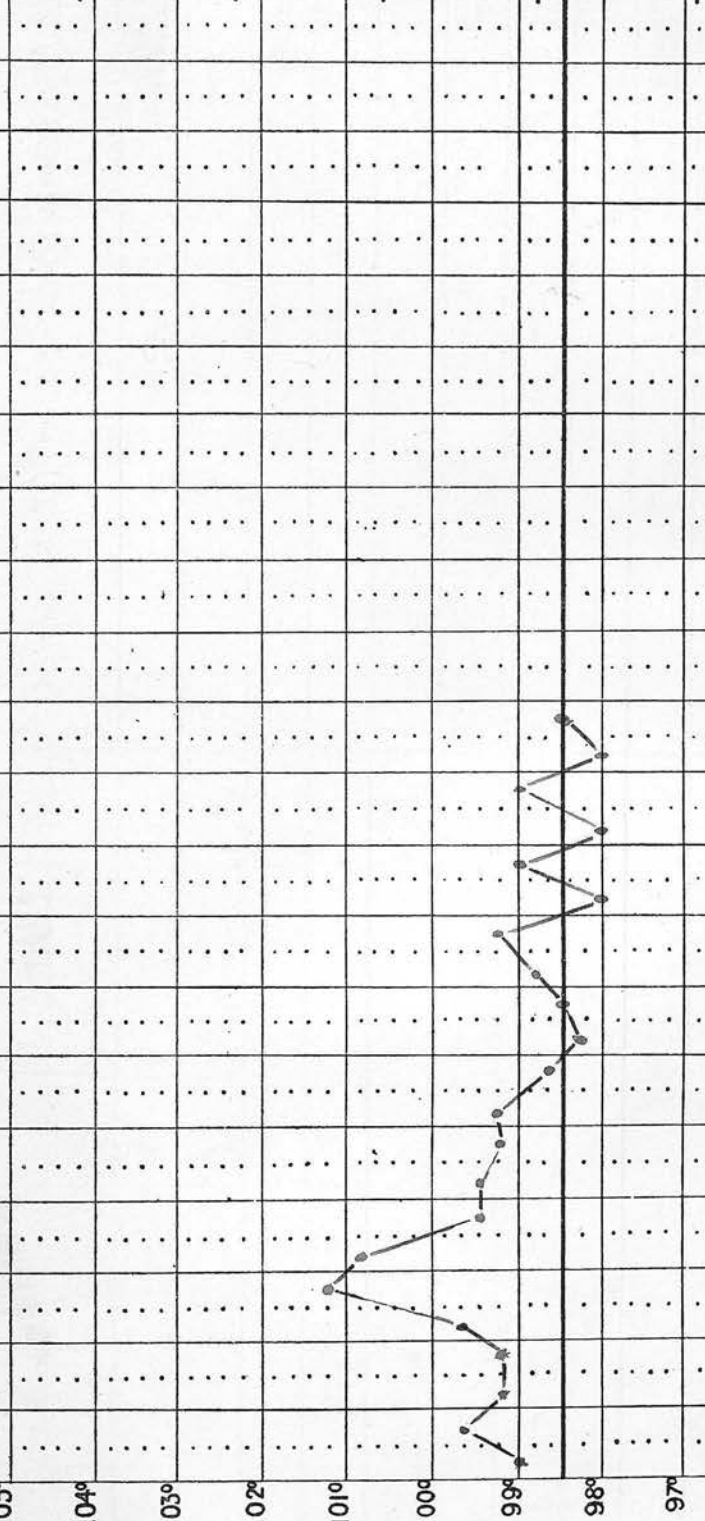
Disease *Scarum*

Result *Cured.*

TEMPERATURE FAHRENHEIT'S SCALE.

TEMPERATURE CENTIGRADE SCALE

36° 37° 38° 39° 40° 41°



Pulse $\frac{m}{\epsilon}$
Resp. $\frac{m}{\epsilon}$
Motions
Urine ozs
Sp Gr.
Reaction
Chlorides
Albumen
Day of Dis.

Pulse $\frac{m}{\epsilon}$
Resp. $\frac{m}{\epsilon}$
Motions
Urine, Ozs
Sp Gr.
Reaction
Chlorides
Albumen
Day of Dis.

Antitoxine Serum
15 cc intramuscular

Temperature 101° ; pulse 126; respiration 44.
 Spinal canal again irrigated with saline, 1500 units of anti-tetanic serum injected intra-durally and 3000 units intra-muscularly.

January 31. 1921. 75 grs. of Potassium Bromide and Chloral Hydrate given t.i.d. Patient's face swollen and there is a marked serum rash distributed all over the body, more markedly on the face.

Slight congestion at the bases of both lungs and a few moist râles heard. General muscular condition unaltered. Bowels well opened.

Temperature 101.8° ; pulse 112; respiration 44.
 No anti-tetanic serum given.

February 1. 1921. Distinct improvement in general condition. Rash unaltered. Taking more nourishment. Rigidity less severe. Mouth can be slightly opened while there are no external stimuli. Clonic muscular spasms have practically ceased. Bowels opened.

Temperature 101.4° ; pulse 102; respiration 32.
 Spinal canal irrigated with saline, 1500 units anti-tetanic serum introduced and 3000 intra-muscularly.

February 3. 1921. General condition further improved.

Spastic condition gradually subsiding. Clonic spasms /

spasms only when stimulated. Serum rash still present. More varied diet given. Bowels well opened.

Temperature 99.2° ; pulse 88; respiration 44. Yesterday no serum given. To-day spinal canal irrigated. 1500 units anti-tetanic serum given intradurally and 1500 intra-muscularly. 5 grains Chloral Hydrate and 10 grains Bromide given t.i.d.

February 7. 1921. Rigidity much diminished and mouth can be opened so that two fingers can be inserted. Clonic spasms have ceased. General appearance of patient much improved.

Temperature 98.6° ; pulse 96; respiration 32. On the 5th instant 1500 units of anti-tetanic serum were given intra-muscularly and 1500 intra-theccally after irrigation. Same repeated to-day.

February 14. 1921. General improvement continues. 1500 units anti-tetanic serum given intra-muscularly on the 10th instant and again to-day.

February 21. 1921. No sign of spasticity. Patient discharged himself to-day.

CASE II.

Name. Annie Myburgh.

Age. 20.

Sex. Female.

Admitted to hospital on February 5. 1917, complaining of "stiff neck".

Previous History. Measles and Scarlet Fever in childhood; fractured right humerus in April 1914.

Family History. Father died of snake bite; otherwise healthy.

Present Complaint. Fourteen days ago patient fell from an apple tree striking her left elbow against the hard garden soil, thereby sustaining a superficial laceration over the left olecranon. She noticed nothing unusual until the day before admission when she complained of stiffness in the region of the neck and right shoulder and a general feeling of malaise. She attended the medical out-patient department and was admitted to hospital.

Examination. Medium built female, well developed. Complexion somewhat pale. Head is held in a slightly retracted position. Movement of the same causes slight pain in the muscles of the neck and are actively resisted. The left shoulder is held in a semi-abducted /

abducted position.

The patient resents passive movements and is disinclined to carry out any active movements, stating that movement causes pain in the shoulder joint and surrounding muscles. There is no swelling in the neck and left shoulder region and no crepitations on movement. The eyes are normal, the pupils reacting well both to light and accommodation.

The teeth are sound and the oral mucous membranes are healthy. The tonsils are small and of normal colour.

No enlarged glands are to be felt in the neck, except for the condition of the left shoulder. The upper extremities are normal. The elbow and wrist reflexes can be elicited. Over the left olecranon there is a small dry scab.

The chest expands well on respiration, the movements being equal on the two sides. The lungs are resonant on percussion. No adventitious breath sounds to be heard. Area of cardiac dullness normal. Heart sounds pure and clear. Abdominal respiration normal. Recti muscles somewhat contracted. On palpation nothing abnormal. Epigastric reflexes brisk.

In the thoraco lumbar region of the spine there is /

is a slight deviation to the left.

All movements are free. The sacro spinalis equally developed on both sides.

On admission the bladder was distended two fingers breadth above the pubis but urine was passed voluntarily after the application of moist heat to the lower abdomen.

Urine specific gravity 1022. Reaction - acid. Albumin - nil. Sugar - nil.

Lower extremities. Movements at all the joints free and not painful. Knee jerks slightly exaggerated on the two sides. Ankle jerks present. Flexor plantar response. No ankle clonus.

Temperature 99.2°; pulse 100; respiration 24.

February 6. 1917. Patient spent a very restless night and during the early hours of the morning her condition became much worse.

She now has an anxious expression and the whole body is bathed in perspiration. The jaw is tightly clenched and cannot be opened, the masseters forming two hard masses, one on each side. The angles of the jaw are retracted, a typical risus sardonicus expression being present. The posterior muscles of the neck and trunk, and the extensors of the lower extremities are in a state of severe spastic contraction /

contraction. The two recti are almost board-like but there is no abdominal tenderness. Severe clonic contractions.

The extensor muscles supersede the tonic condition, throwing the patient in the opisthotonos attitude.

Temperature 104° ; pulse 120; respiration 30. The condition is now diagnosed as tetanus.

Patient is now given a $\frac{1}{4}$ grain of morphia, and a general anaesthetic administered. Lumbar puncture is performed in the third lumbar space. 25 cc. of cerebro-spinal fluid drained off and an equal quantity of saline solution reinjected. The position of patient is altered so as to bring the saline solution into an intimate mixture with the cerebro-spinal fluid. The lumbar needle is left. 25 cc. of the fluid again drawn off and the above process repeated five times. 1500 units of anti-tetanic serum is introduced into the thecal space and the needle withdrawn. 3000 units are given intra-muscularly. The bowels are cleared by means of an enema, a copious result being obtained.

A solution of 20 grains Chloral Hydrate and Bromide is given per rectum.

February 7. 1917. Patient is being kept deeply under /

under the influence of morphia and Chloral, all external stimuli being shut off as far as possible. The spastic condition unaltered, but the clonic spasms are somewhat diminished in frequency and intensity.

Pulse 120; respiration 27; temperature 103° .

Chloroform anaesthetic induced and lumbar puncture performed. The irrigation of the spinal canal is carried out the same as yesterday, 1500 units of anti-tetanic serum again being introduced intra-theccally and 3000 intra-muscularly.

February 8. 1917. There is no marked general improvement to-day. The spastic and clonic states continue as before. Bowels opened by an enema. Fluid nourishment given through a feeder. 10 grains of Chloral Hydrate and Bromide given t.i.d. Temperature 101° ; pulse 128; respiration 24. General anaesthetic administered. Spinal canal irrigated with saline. 1500 units anti-tetanic serum introduced intra-theccally. 3000 units into buttock.

February 10. 1917. Although the spastic condition of the muscles still remains severe, the clonic spasms have practically ceased, only taking place on strong stimulation. Patient still has to be fed by means of a feeder and tube. Chloral Hydrate and Bromide reduced to 5 grains each t.i.d.

No serum was given yesterday. Under a general anaesthetic the spinal canal was again irrigated today, 1500 units of anti-tetanic serum given intrathecally and 3000 units into the buttock intramuscularly.

February 14. 1917. On the 12th inst. spinal canal was irrigated as before, 1500 units anti-tetanic serum injected intrathecally and 1500 units intramuscularly.

For the last 48 hours the patient has had no clonic spasms. There is still some spasticity of the muscles of the trunk. The spasms of the masseters are somewhat relieved, the patient being able to open the jaw slightly.

The bowels now act voluntarily. Temperature 99.8°; pulse 100; respiration 24. Chloral Hydrate and Bromide are continued. After irrigation of the spinal canal 1500 units of anti-tetanic serum are introduced and an equal quantity into the buttock.

February 16. 1917. General improvement continues and spastic state gradually subsides. Spinal canal is again irrigated with saline, 1500 units given intrathecally and 1500 units given intramuscularly. Patient is given some solid food.

February 19. 1917. There is still slight stiffness /

stiffness of the neck and back and obvious stiffness of the masseters.

Temperature 99°; pulse 96; respiration 22.

1500 units of anti-tetanic serum given intra-muscularly.

February 23. 1917. Except for very slight stiffness of the jaw the rigidity of the muscles has now passed off. Temperature, pulse and respiration are now normal. 1500 units of anti-tetanic serum given intra-muscularly. Chloral and Bromide are discontinued.

March 5. 1917. The patient is discharged as cured.

CASE III.

Name. Abraham Truter.

Age. 14.

Sex. Male.

Admitted to hospital, May 18. 1921, complaining of a lacerated injury of the left hand.

Previous History. Measles, diphtheria some years previous.

Family History. Unimportant.

Present Complaint. While working with a forage cutter, patient's hand was drawn in between two cogged rollers and badly lacerated.

Examination. Well built youth in a slightly shocked condition. Heart, lungs and abdominal organs normal.

On the dorsum of the hand the skin is lacerated and bruised. On the volar aspect of the index and middle fingers there are two cuts extending to the bones of the middle phalanges.

The metacarpals of the index, middle and ring fingers are communicated. Forage and dust are ground into the wounds. The wounds are cleaned as far as possible and devitalised tissue removed by means of scissors. The hand is put on an anterior metal splint and frequent eusol compresses applied.

May /

May 26. 1921. General condition of patient good.

The hand is septic but gradually improving under eusol baths and hot fomentations.

June 4. 1921. The patient who has been more or less comfortable up to the present, to-day developed stiffness of the jaw.

The jaw is clenched but can be opened to admit one finger.

The angles of the mouth are retracted.

The patient complains of slight stiffness of the neck but movements are free.

Abdomen soft, bowels and bladder are regular.

Knee jerks are slightly exaggerated. Patient is irritable and is sweating profusely.

Temperature 102.2°; pulse 108; respiration 24.

It not being known whether the patient previously had anti-diphtheric serum, the patient was only given $\frac{1}{2}$ cc. of anti-tetanic serum, $\frac{1}{6}$ grain Morphia hypodermically and per os 15 grains of Chloral Hydrate and Bromide 15 grains.

June 5. 1921. The general condition of patient remains the same; the masseters are perhaps a little more tense.

After the test injection of serum there was no reaction.

Lumbar /

Lumbar puncture is performed in the 3rd lumbar space and 25 cc. of cerebro-spinal fluid withdrawn.

25 cc. of sterile normal saline is injected. Patient is tilted from side to side and up and down to allow mixing of cerebro-spinal fluid and saline.

25 cc. of fluid again withdrawn and the above process repeated five times.

1500 units of anti-tetanic serum injected intrathecally and 1500 units given into the gluteal region. 10 grains each of Chloral Hydrate and Pot. Bromide given t.i.d.

Temperature 102° ; pulse 108; respiration 24.

June 6. 1921. Patient had a slight clonic spasm last night.

This morning condition is unaltered. Temperature 102° ; pulse 120; respiration 32. 1500 units anti-tetanic serum are given intra-muscularly.

June 7. 1921. Considerable improvement in patient's condition; the spastic condition of jaw is greatly diminished.

Temperature 100.6° ; pulse 100; respiration 26. The spinal canal again irrigated with saline solution.

1500 units anti-tetanic serum given intrathecally and 1500 units intra-muscularly. 5 grains Chloral Hydrate and 5 grains Potassium Bromide t.i.d.

June /

June 12. 1921. There is to-day no spastic condition of the jaw, patient being able to open mouth freely.

The stiffness of the neck has completely passed off.

Patient has been up and about for two days already.

Pulse, temperature and respiration are normal.

June 15. 1921. Patient discharged as cured.

FINAL SUMMARY.

- I. The object of these experiments was primarily to find the influence of the central nervous system on the development of tetanus rigidity and to locate which centres take part in the pathogenesis of the characteristic symptoms.
- II. The place of injection had no effect on the distribution of the stiffness. Extensor stiffness resulted whether the injection was made in flexor or extensor muscles.
- III. The position of the limbs before the development of the stiffness was also without influence.
- IV. Experiments of hemi-sections of the cord showed that the supra-spinal centres have an influence on the development of rigidity. The extensor stiffness of local tetanus is less marked on the operated side when injections are made in both hind legs.
- V. One of the centres which give to the spinal cord the permanent innervation which is necessary for the development of the normal degree of extensor rigidity is the cerebellum. After an extirpation of this centre, extensor rigidity will /

will develop, also on the homo-lateral side, but the degree of rigidity is less than on the non-operated side when bilateral injections are given into the hind legs.

VI. Destruction of the cerebral cortex produced no effect upon the manifestation of tetanus intoxication.

VII. Uni-lateral destruction of the corpus striatum preceding injections of tetanus toxin in both hind legs resulted in flexor rigidity instead of the normal extensor rigidity. This was on both sides, but was more marked on the homo-lateral one.

VIII. These facts suggest that the corpus striatum has also in normal life an influence on the distribution of tonus.

IX. In treatment of tetanus the method to be preferred is to combine intra-theal injections of anti-toxin with washing out of the sub-arachnoidal space.

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